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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,008	07/31/2003	Avi Ashkenazi	39766-0100P1	8996

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Ginger R. Dreger, Esq.
HELLER EHRMAN WHITE & MCAULIFFE, LLP
275 Middlefield Road
Menlo Park, CA 94025

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/633,008	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/28/05, is acknowledged.

2. Claims 7-15 are pending and under examination as they read on a method of treating an inflammatory disorder with an immunoadhesin comprising the extracellular domain sequence of SEQ ID NO: 32 and the species of rheumatoid arthritis.

3. Figures 25-26 stands objected to because applicant has not affirmed whether the figures depict in situ hybridization or immunohistochemistry graphs. Clarification/Correction is required.

4. In view of the amendment filed on 11/28/05, only the following rejection is remained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 7-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing the progression of rheumatoid arthritis in mammal comprising administering to said mammal an effective amount of an immunoadhesion comprising the extracellular domain sequence of the polypeptide of SEQ ID NO:32 , does not reasonably provide **enablement** for a method of treating any "inflammatory disorder" in a mammal, comprising administering to said mammal an effective amount of an "immunoadhesin" comprising an extracellular domain sequence of polypeptide of SEQ ID NO: 32 in claim 7, wherein said immunoadhesin comprises a "said extracellular domain sequence fused to an immunoglobulin constant region sequence" in claim 8, wherein said extracellular domain sequence is "essentially free of transmembrane domain sequences" in claim 9, wherein said immunoglobulin is an IgG in claim 10, wherein said IgG is IgG1 or IgG3 in claim 11, wherein the inflammatory disorder is rheumatoid arthritis in claims 11 and 12, wherein said mammal is human in claims 14 and 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 5/26/05.

Applicant's arguments, filed 11/28/05, have been fully considered, but have not been found convincing.

Applicant asserts that the extensive experimental data provided in the specification clearly establish that STIgMA mRNA and protein expression are associated with a large variety of inflammatory conditions in humans and demonstrate that an inflammatory condition characterized by elevated STIgMA levels (rheumatoid arthritis) can be successfully treated by administration of STIgMA-Ig-immunoadhesion in a relevant animal model.

At issue is whether or not the claimed antibody would function to treat any "inflammation". The specification discloses that systemic injection of the STIgMA fusion protein muSTIgMA-Fc, into collagen-induced arthritic mice resulted in a significant reduction in the progression of CIA compared to a control group of mice treated with IgG1 (Figure 71 in particular). Further the specification discloses that the expression of STIgMA in macrophases significantly increased in the presence of pro-inflammatory cytokines, high expression levels of STIgMA mRNA were found in alveolar macrophases obtained from lung autopsy of human patients with pneumonia and chronic asthma, and in Kupffer cells of a human patient with chronic hepatitis (figure 63A-F), high expression levels of STIgMA mRNA were found in synovial cells obtained from a human patient with osteoarthritis (figures 64A-D), expression of STIgMA protein was confirmed in the synovial of human patient with rheumatoide arthritis, while STIgMA was absent in control synovium (Fig. 65A-D). The exemplification is drawn to reduction of the progression of CIA that received the STIgMA fusion protein, in an assay that measure anti-collagen type II antibody titer, radiographs, 5CT and histophathology methods (see example 25).

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since CIA animals were used as model system to treat rheumatoid arthritis. Walker (of record) teaches that the Z39Ig gene has no known function. It is not clear that reliance on such data of CIA animal model accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. Besides rheumatoid arthritis, the specification does not adequately teach how to effectively treat any inflammatory disorder or reach any therapeutic endpoint in mammals by administrating the therapeutic composition. The specification does not teach how to extrapolate data obtained from an in CIA model studies to the development of effective in vivo mammalian therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the therapeutic package exemplified in the specification.

However, an effective protocol for the treatment of inflammatory disorder in mammalian is subject to a number of factors which enter the picture beyond simply the administration of the therapeutic composition in an acceptable formulation. Demonstrating a correlation between CIA and reduction in the progression of CIA cannot alone support the predictability of the method for treating any inflammatory disorder through administration of the appropriate formulation. The ability of a host to suppress and thereby treat inflammation will vary depending upon factors such as the condition of the host and burden of disease. While the specification discloses that the expression of STIgMA in macrophages significantly increased in the presence of pro-inflammatory cytokines, and high expression levels of STIgMA mRNA were found in alveolar macrophages obtained from lung autopsy of human patients with pneumonia and chronic asthma and in Kupffer cells of a human patient with chronic hepatitis among other, Kim et al teaches that the Z39Ig protein (claimed STIgMA protien) may be involved in mediating phagocytosis and/or antigen presentation. Importantly, the specification fails to identify a ligand that would bind to STIgMA which would lead to the increased in the presence of the pro-inflammatory cytokines. The function of the STIgMA is unknown (Walker) and its ligands are also unknown, thus undue experimentation would be required to practice the claimed methods with a reasonable

expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective in an inflammatory disorder.

Walker teachings that Z39Ig protein (claimed STIgMA) is a cell surface receptor (see abstract) appears to be at odds with the Applicant's disclosure that PRO362 protein (claimed STIgMA) is a secreted protein (see paragraph 114) i.e., a ligand. Since the instant claims were drafted based on the specification disclosure, the skilled artisan still would not have a reasonable expectation that the claimed method would lead to a desirable endpoint of treating any inflammation disorder in the subject.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 17, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner